DEPARTMENT OF HEALTH AND HUMAN SERVICES

FEI: 1119643

Food and Drug Administration
Baltimore District Office
6000 Metro Drive
Suite 101
Baltimore, MD 21215-3215
Telephone: (410) 779-5454

March 10, 2005

WARNING LETTER
05200106

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Mark D. Boivin, President
DanChem Technologies, Inc.
P.O. Box 400
Danville, VA 24543

Dear Mr. Boivin:

From September 20 to October 5, 2004 the Food and Drug Administration conducted inspections of your Active Pharmaceutical Ingredient (API) manufacturing facility located at 1975 Old Richmond Road, Danville, VA 24540. The inspection resulted in the issuance of a 5 item FDA-483 at the completion of the inspection. A second inspection was conducted on November 9, 2004 in order to collect additional records.

The inspections documented the interstate shipment of at least seven lots of calcium polycarbophil active pharmaceutical ingredient (API) which your customer's analyses demonstrated were contaminated with physical filth causing them to be adulterated within the meaning of Section 501(a)(1) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 351(a)(1)).

The inspections also documented significant violations of current good manufacturing practice (cGMP) in the manufacturing of active pharmaceutical ingredients. The deviations also cause these APIs to be adulterated within the meaning of Section 501(a)(2)(B) of the Act (21 U.S.C. 351(a)(2)(B)). While this inspection did not cover the manufacture of your Irgasan PG60 active pharmaceutical ingredient, used in the manufacture of antibacterial soaps, Section 501(a)(2)(B) requires that all drugs be manufactured, processed, packed, and held in accordance with current good manufacturing practice.

Examples of your firm's failure to follow cGMP in API production include, but are not limited to, the following:

1. Out-of-specification (OOS) batches of calcium polycarbophil were blended with other batches for the purpose of meeting specifications. Four batches of out-of-specifications calcium polycarbophil API were blended with other lots and then distributed.

2. Batch records do not include the name and weight of all components used in the course of production. Specifically, a member of your management ordered employees to add out-of-specification batches to new batches being manufactured. The addition of the out-of specification material to the new batches is not documented in the batch records.

3. Records documenting the disposal of rejected and out-of-specification calcium polycarbophil API are not accurate in that a member of your management ordered employees to fill containers labeled as rejected API with other material and debris, seal the containers, and dispose of them as if they still contained the rejected API.

4. Batch record reviews of multiple batches failed to detect unexplained discrepancies when the rate of production exceeded the capabilities of the processing equipment.

5. Failure to conduct and document an investigation when foreign material was observed in the manufacturing equipment during the processing of calcium polycarbophil. Subsequently, 40 batches of calcium polycarbophil were recalled due to the same foreign material.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your API is manufactured in compliance with the Act and cGMPs. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's quality system. You are responsible for investigating and determining the cause of all inspectional observations listed in the Form FDA-483 issued to you.

We acknowledge receipt of your letter dated October 6, 2004. In that letter you outline corrective actions such as the creation of a new GMP manager position, dedication of operators to the GMP plant in addition to the dedicated equipment system already in place, personnel retraining as well as equipment and procedure changes. While these are positive actions on your part, your response is general in nature. We remain concerned that the underlying system problems resulting in the violations have not been fully addressed. Given the serious nature of the violations more information about your actions is necessary before we can consider your response adequate.

Observations 1 and 4 on the Form FDA-483 are related and concern the re-blending of four OOS lots of calcium polycarbophil, designated for destruction, into new lots being manufactured. Your response indicates that "off-specification material" will be locked in a quarantine area. You state later that "reprocessing procedures will be written and validated as needed" without further elaboration. While it may be possible to reprocess OOS material, be advised that it is unacceptable to blend such material into acceptable material or material which is not yet tested for the purpose of diluting out the defect. Please explain if your company intends to reprocess OOS material and what types of OOS lots would be eligible. Please describe in detail the reprocessing procedures and how you intend to validate them. Alternatively, you may submit the procedures and validation protocol(s) and report(s). Also, we expect that investigations into the original failures, e.g., low calcium or high moisture, have been completed and preventive action implemented to preclude such failures in the future.

We do not find your response regarding the contamination of your API with foreign matter adequate. Your response to Observation 3 describes means to find foreign matter or screen it out such as modifying the sifter screen to prevent foreign matter from entering the finished product drum. However, we also expect drug manufacturing procedures and equipment to be designed to prevent introduction of foreign matter during processing to the extent that is possible and reasonable. Given the variety of foreign matter found in your product, it does not appear that your present system provides adequate protection to the product during processing. Please comment on what actions you will take to prevent this foreign matter from getting into the API during all stages of manufacturing.

You indicate that you have retrained operators and supervisors and that "overs" or overflow material will not be charged back into the blender. Please explain why you believe the overflow material is a source of the contamination. Also, we assume your personnel were previously trained and yet gross contamination with latex gloves, wood, paper, string occurred anyway. We are not convinced you can prevent such occurrences again until your company has identified how and why this foreign matter was introduced during manufacturing.

Your response does not address your procedures for conducting investigations in response to OOS test results, foreign matter, batch record discrepancies or other unanticipated incidents. Please elaborate and submit copies of your investigation procedure(s).

Your corrective actions to your quality system must be sufficient to ensure your quality system is able to prevent and detect future violations of a similar nature as those cited on the Form FDA-483.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and prosecution.

Please notify this office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted GMP violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Include all the documentation of the corrective actions you have taken. If the corrective actions cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to Mr. Steven B. Barber, Compliance Officer, Food and Drug Administration, 6000 Metro Drive, Suite 101, Baltimore, MD 21215. If you have any questions, please contact Mr. Barber at (410) 779-5134.

Sincerely yours,

Lee Bowers
District Director
Baltimore District